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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/623,640	07/21/2003	Tao Guo	1073.071	5187

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EXAMINER

BERNHARDT, EMILY B

ART UNIT PAPER NUMBER

1624

DATE MAILED: 06/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/623,640	GUO ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Emily Bernhardt	1624	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 13-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12 and 19-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>7/21/03</u> . | 6) <input type="checkbox"/> Other: ____.  |

Restriction to one of the following inventions is required under 35 U.S.C.

121:

- I. Claims 1-12 and 19-21, drawn to compounds, compositions and uses where A= formula II or III, classified in classes such as 540,544,548, subclasses 492,385,319.1 respectively and others as may be determined by the nature of substituents thereon; class 514, subclasses 218, 255.02, 392,etc.
- II. Claims 1,2,13,14, and 19-21, drawn to compounds, compositions and uses where A=formula IV, classified in class 540,546,548, subclasses 527,216,550 respectively and class 514 subclasses 212.03, 327,424,etc.
- III. Claims 1,2,16-21, drawn to compounds, compositions and uses where A=formula V, classified in classes such as 560, subclass 27; class 564, subclasses 56,153,etc.; class 514 subclasses such as 487,595, 616.

In addition to an election of one of the above groups, applicants must elect a single species embrative of said group. Based on species elected, corresponding "A" ring will be held as constructively elected.

The inventions are distinct, each from the other because:

Compounds within I-III are drawn to a variety of dissimilar compounds that are variously classified in view of the choices permitted at A which permit an assortment of 5-7 membered rings or acylated amino chain for group III. Such compounds are not art-recognized equivalents in general much less in the art to which the instant invention pertains. Art which may anticipate one of these groups would not necessarily do the same for those remaining in view of the structural dissimilarity of compounds of I vs II vs III as a whole. Within groups I and II there is more than one invention as the A rings can be triazine, tetrazine, diazepine, imidazolidione, piperidinone, azepinone, or pyrrolidone- all separately classified and requiring separate online searches and thus need to be further restricted.

During a telephone conversation with Mr. Hansen on 6/9/04 a provisional election was made with right of traverse to prosecute the invention of I, claims 1-12,19-21 and species of eg.42 in particular. Affirmation of this election must be made by applicant in replying to this Office action. Claims 13-18 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

In view of the election of eg.42, the A ring being examined will be limited the piperazinedione ring in formulas II and III where  $V=C$ ,  $W=C$  and  $n=1$ . Claims

which link the various inventions will only be examined with respect to the elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The disclosure is objected to because of the following informalities: On p.85 the structure in eg.23 is superimposed on the title.

Appropriate correction is required.

Claims 1-5,10-11,19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. In the definitions (ii) and (iii) what is the significance of “*n*” appearing after “(C<sub>1</sub>-C<sub>6</sub>)” ? Is it intended to mean “normal” alkyl or something else?

Claims 20-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled

in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Method claims 20 and 21 for treating infertility and preventing conception are not enabled based solely on specification's description that instant compounds can be used as partial agonists or antagonists of the FSH receptor. Note the criteria for enablement as set out in *In re Wands* cited in MPEP 2164.01(a), August 2000 edition, which includes factors such as:

1) Breadth of the claims- The claims cover compounds easily in the millions;

2) Level of unpredictability in the art- The invention is pharmaceutical in nature involving activity at a particular receptor (FSH). It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved" and physiological activity is generally considered to be unpredictable. See *In re Fisher* 166 USPQ 18. The Guo publication published after applicants' filing date evidences activity is sensitive to structure at various locations of the piperazinedione ring. See discussion beginning on p.1719 of the publication, provided herewith;

3) Direction or guidance- The amount of guidance presented in the specification as to which compounds are sufficiently active to be useful for the

claimed uses is nonexistent. The dosage range information ( on p.9) is virtually useless being a 250,000 fold range and not directed to a specific disease;

4) State of the prior art- The compounds are bis-aryl piperazinediones with a certain substitution pattern at variables X,Y,Z or T on the "Ar" ring. No such compounds are known in the prior art having the instant activity;

5) Working examples- No test data has been presented only description of assay testing protocols and thus it is by no means clear how active these compounds actually are. Thus in the absence of animal studies and in the absence of any correlation between studies conducted **in vitro** and the diseases to be treated, there is no sufficient evidence to support the claimed uses.

In view of the above considerations, this rejection is being applied.

Claims 1-12 and 19-21 are rejected under judicial doctrine as being drawn to an improper Markush group. The Markush at "A" covered by these groups are not art-recognized equivalents and there is no evidence of record that the remaining biphenyl ring common to the compound groups contribute solely to the instant physiological activities. Note In re Milas 71 USPQ 212 in which the structural difference between vitamin A and D was sufficient to uphold the improper Markush rejection. Also see In re Winnek 73 USPQ 225 and In re Ruzicka 66 USPQ 226 in which structural differences were small and yet a similar holding was

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maintained. All these cases involved compounds in the pharmaceutical art known to be structure-sensitive.

Deletion of nonelected subject matter would overcome this rejection.

A search in the pertinent art area resulted in nothing teaching or suggesting the structural makeup of piperazinediones claimed herein.

Was the proviso appearing in claim 1 (see X-Z definition in (i)) necessitated by prior art? If so, its identification is requested to complete the record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is (571) 272-0664.

If attempts to reach the examiner by phone are unsuccessful, the supervisor for AU 1624, Dr. Mukund Shah, can be reached at (571)272-0674.

The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

  
**EMILY BERNHARDT**

**PRIMARY EXAMINER**

**Group 1600**